

14.0 GLOSSARY¹

Accuracy²: A measure of test performance. (a) The closeness of agreement between a test result and an accepted reference value; (b) The proportion of correct outcomes of a method. Often used interchangeably with **concordance**.

Activation (of genes): The interaction of specific molecules or molecular complexes with specific genes to initiate their expression (transcription of mRNA).

Affinity (high; low): The strength of binding of a molecule to a receptor protein.

Agonism: The binding of a substance to a receptor to initiate effects similar to those produced by the natural ligand for the receptor.

Agonist: A substance that mimics the action of an endogenous hormone.

Androgen: A class of steroid hormone, which includes testosterone and 5 α -dihydrotestosterone, responsible for the development and maintenance of the male reproductive system.

Antagonism: The binding of a substance to a receptor to inhibit or counteract the effects produced by the natural ligand for the receptor.

Antagonist: A substance that blocks or diminishes the activity of an **agonist**.

Cell-free: Not containing intact cells. May contain cell or tissue homogenates or artificial mixtures of cellular components.

¹ The definitions in this Glossary are restricted to their uses with respect to endocrine mechanisms and actions.

² Definition used by the Interagency Coordinating Committee on the Validation of Alternative Methods.

Complex mixture: A mixture containing many, generally uncounted, substances, many of which are undefined (e.g., plant homogenates; fuels).

Concordance²: A measure of test performance. The proportion of all chemicals that are correctly classified as positive or negative. Often used interchangeably with **accuracy**. The concordance is highly dependent on the **prevalence** of positives in the population being examined.

C-Terminal region: The end of a protein molecule that contains a free carboxylic acid moiety.

Cytoplasm: The material inside the cell, excluding the nucleus, that contains the intracellular fluid, organelles, soluble enzymes, membrane components and other factors.

Cytosol: see Cytoplasm

Detoxification: Reduction of the toxicity (of a substance) by metabolism to a less toxic form, or by removal of the substance from the affected cell or organism.

Dextran: A viscous or semi-viscous polymer of glucose.

Dissociation constant: A measure of the ability of a molecule to be released from binding to a receptor.

DNA-regulatory activity: Refers to a DNA-binding molecule or complex that causes a change in DNA-related activities.

Domain: A region of a protein defined by its activity.

Endocrine disruption: Activity by an exogenous chemical substance that alters the structure or function(s) of the endocrine system and causes adverse effects at the level of the organism, its progeny, populations, or subpopulations of organisms.

Endocrine disruptor: A substance determined to cause endocrine disruption.

Endocrine system: Made up of glands located throughout the body, the hormones that are synthesized and secreted by the glands into the bloodstream, and the receptors in the various tissues are organs that recognize and respond to the hormones.

Endogenous: Originating within the organism of interest.

Endpoint: The biological process, response, or effect assessed by a test method.

Estrogen: A class of steroid hormones, which includes 17 β -estradiol, responsible for regulation of specific female reproductive functions and for development and maintenance of the female reproductive system.

Estrogenic: Having biological activity similar to that of an estrogen.

Exogenous: Originating outside the organism of interest.

False negative²: An active substance incorrectly identified as negative by a test.

False negative rate²: The proportion of all positive (active) substances falsely identified as negative. A measure of test performance.

False positive²: An inactive substance incorrectly identified as positive by a test.

False positive rate²: The proportion of all negative (inactive) substances falsely identified as positive. A measure of test performance.

Fluorescence polarization (FP): A technique that can detect molecular interactions by monitoring changes in the polarization of fluorescently labeled or inherently fluorescent molecules.

Frog metamorphosis assay: A test method that measures the ability of a substance to affect the metamorphosis of frog larvae (tadpoles) to adults.

Gonadal recrudescence assay: A test method that measures the ability of a substance to produce effects in estrogen- and androgen-dependent accessory sex organs or gonad maturation in fish. A test method for potential estrogen- and androgen-related endocrine disruption.

Half-life: The time it takes for a chemical or radioactive substance to lose half its activity.

Hazard: An adverse health or ecological effect.

Hershberger assay: Measures the ability of a substance to alter the weight of androgen-dependent accessory sex organs (e.g., ventral prostate or seminal vesicles) or tissues in castrated rats or mice. A test method for potential androgen and anti-androgen related endocrine disruption activity.

Homology (DNA): Similarity in DNA sequence of segments or genes from different strains or species of organisms.

Hormone: A chemical substance produced in specific cells, or glands, that can either act locally or be released into the bloodstream to act on an organ or tissue in another part of the body.

Hydrophobic: Refers to chemicals and substances that will not dissolve or that sparingly dissolve in water.

Hydroxyapatite (HAP): A form of calcium phosphate with the ability to bind to some classes of organic molecules.

Hypospadias: A clinical condition in newborns that manifests itself as a displaced opening of the urethra. Occurs in males only and is considered a fetal developmental anomaly.

Interlaboratory reproducibility²: A measure of whether different laboratories using the same protocol and test chemicals can produce qualitatively and quantitatively similar results. See **reliability**.

Intralaboratory reproducibility²: A measure of whether the same laboratory can successfully replicate results using a specific test protocol at different times. See **reliability**.

Intraperitoneal: Administration by injection directly into the peritoneal cavity.

In vitro: In glass. Refers to assays that are carried out in an artificial system (e.g., in a test tube or petri dish) and typically use single-cell organisms, cultured cells, cell-free extracts, or purified cellular components.

In vivo: In the living organism. Refers to assays performed in multicellular organisms.

K_d: Equilibrium dissociation constant of a reference compound in a specific receptor preparation. A measure of the strength of binding between a receptor and ligand.

K_i: Equilibrium dissociation constant of an inhibitor in a competitive receptor binding experiment.

Ligand: A substance that is capable of binding to a specific receptor protein.

Ligand-binding domain: The area within a receptor molecule that attracts and holds a ligand.

Metabolic activation: Metabolism of a chemical by an organism or a cell-free extract to a biologically active form.

Negative control: An untreated sample containing all reagents of a test system, except the assay solvent, which is replaced with a known non-reactive material, such as water. This sample is processed with treated samples and other control samples to determine whether the solvent interacts with the test system.

Negative predictivity²: The proportion of correct negative responses among substances testing negative.

N-Terminal region: The end of a protein molecule that contains a free amino acid moiety.

Ovariectomized: Having the ovaries surgically removed.

Peer review: Objective review of data, a document, or proposal, and provision of recommendations, by an expert individual or group of individuals having no conflict of interest with the outcome of the review.

pH: A measure of the acidity or alkalinity of a solution. pH 7.0 is neutral; higher pHs are alkaline, lower pHs are acidic.

Placental aromatase assay: Measures the ability of a substance to induce or inhibit the activity of the aromatase enzyme, which converts testosterone to estradiol. A test method for potential anti-estrogen related endocrine activity.

Positive control: A sample containing all components of a test system and treated with a substance known to induce a positive response, that is processed with other samples to demonstrate the sensitivity of each experiment and to allow for an assessment of variability in the conduct of the assay over time.

Positive predictivity²: The proportion of correct positive responses among substances testing positive.

Prevalence²: The proportion of positives in the population of substances tested.

Priority setting: The collection, evaluation, and analysis of existing relevant information to determine whether, and in what relative order of priority, substances will be subjected to screening or testing.

Protocol²: The precise, step-by-step description of a test, including the listing of all necessary reagents, criteria and procedures for the evaluation of the test data.

Pubertal female assay: Measures the ability of a substance to induce or inhibit the onset of puberty in immature female rats and mice, measured as an early or late opening of the vagina. A test method for potential estrogenicity and anti-estrogenicity.

Pubertal male assay: Measures the ability of a substance to induce or inhibit prepubertal separation in immature male rats and mice. At recovery (53 days), various tissues are weighed and the thyroid examined histologically. A test method for potential androgen- and anti-androgen related endocrine disruption.

Radiolabel: A radioactive isotope of an atom that is added to a molecule to allow the molecule to be identified by **scintillation counting**.

Receptor: A protein or protein complex, which binds to specific molecules for the purpose of transporting them elsewhere in the cell, or for producing a chemical signal.

Receptor binding assay (competitive): An assay to measure the ability of a substance to bind to a hormone receptor protein, which is typically performed by measuring the ability of the substance to displace the bound natural hormone.

Receptor superfamily: A family of related receptors with similar composition and reactivity (e.g., the estrogen, androgen, and glucocorticoid receptors).

Relevance (of an assay)²: The relationship of a test to the effect of interest and whether a test is meaningful and useful for a particular purpose. The extent to which an assay will correctly predict or measure the biological effect of interest. A measure of assay **performance**.

Reliability (of an assay)²: The intra- and inter-laboratory **reproducibility** of the assay.

Repression (of genes): The interaction of specific molecules or molecular complexes with specific genes to prevent their expression (transcription of mRNA).

Scintillation counting: The measurement of radioactivity using a scintillation counter.

Screen/Screening Test²: A relatively rapid, simple test conducted for the purposes of a general classification of substances according to general categories of hazard. The results of a screen are generally used for preliminary decision-making and to set priorities for more definitive tests. A screening test may have a truncated response range (e.g., provides a qualitative response only).

Sensitivity²: The proportion of all positive substances that are correctly classified as positive in a test.

Solvent control: An untreated sample containing all components of a test system, including the solvent, that is processed with treated samples and other control samples to determine whether the solvent interacts with the test system.

Specificity²: The proportion of all negative substances that are correctly classified as negative in a test.

Stereospecific: Refers to the orientation of atoms within a molecule. The specific orientation of some atoms can affect the chemical reactivity of the molecule.

Steroidogenesis assay: Measurement of the ability of chemicals to inhibit steroid hormone biosynthesis in testicular tissue or cells *in vitro*.

Sulfhydryl: Chemical containing sulfur in the form of a -SH group.

Test battery: A series of tests, usually performed at the same time or in close sequence. Each test in the battery usually measures a different component of a multifactorial toxic effect, or a mechanistically-related effect.

Tier 1 assay for endocrine disruptors: An assay that is a component of the EDSP screening battery of tests.

Tier 1 battery for endocrine disruptors: Defined by the EDSP as a series of *in vitro* and *in vivo* tests to determine the ability of substances to interact with the endocrine system.

Tier 2 assay for endocrine disruptors: An assay that is a component of the EDSP testing battery.

Tier 2 battery for endocrine disruptors: Defined by the EDSP as a series of *in vivo* tests designed to confirm the endocrine disrupting ability of substances in laboratory animals and wildlife species.

Transcriptional activation: The initiation of mRNA synthesis in a gene in response to a specific chemical signal, such as an estrogen-estrogen receptor complex.

Transcriptional regulatory protein: A protein that binds to a specific DNA sequence resulting in a change in the regulation of mRNA synthesis.

Uterotrophic assay: Measures the ability of a substance to cause uterine enlargement in an immature or ovariectomized rat or mouse. A test method for potential estrogenicity and anti-estrogenicity.

Valid method²: A method determined to be acceptable for a specific use.

Validated method²: A method for which the reliability and relevance for a specific purpose has been established.

Validation²: The process by which the reliability and relevance of a procedure for a specific purpose are established.

Vector: A small segment of DNA (frequently a plasmid or viral DNA) that is used to carry a foreign gene or DNA sequence into a cell's nucleus.

Weight of evidence (process): The strengths and weaknesses of a collection of information are used as the basis for a conclusion that may not be evident from the individual data.

Xenobiotic: A substance that is not produced by the organism of interest.

Zinc finger motif: A configuration of a DNA-binding protein that resembles a finger and binds a zinc ion for its activity.